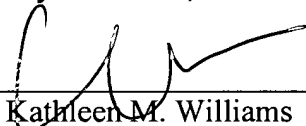## REMARKS

The Amendments directed herein are made in order to make the specification agree with the form of the Formal Figures submitted herewith. For clarity and in order to comply with U.S.P.T.O. rules regarding figures, the Formal Figures have been amended to change the scheme for indicating the location and identity of mutations in Figures 14 and 15.

In Figures 14 and 15, underlining of mutated residues in sequence printed on a regular white background is used instead of the dark shading of invariant residues and non-shading of mutated residues used in the figures as originally filed. Copies of the original Figures 14 and 15, plus clean and marked-up versions of amended Figures 14 and 15 are submitted herewith.

The amendments add no new matter. Entry of the amendments to the specification and Figures is respectfully requested. Entry of the Formal Figures as amended is also requested.

Respectfully submitted,

Date: _____\1\1\22\04_____

_____
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Customer No.: 27495
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Boston, MA 02199-7613
Tel. (617) 239-0100

ATGATCCTTGACGTTGATTACATCACCGAGAATGGAAAGCCCGTCATCAGGGTCTTCAAGAAGGAGAACGGC
GAGTTCAGGATTGAATACGACCGCGAGTTCGAGCCCTACTTCTACGCGCTCCTCAGGGACGACTCTGCCATC
GAAGAAATCAAAAAGATAACCGCGGAGAGGCACGGCAGGGTCGTTAAGGTTAAGCGCGCGGAGAAGGTGAAG
AAAAAGTTCCTCGGCAGGTCTGTGGAGGTCTGGGTCCTCTACTTCACGCACCCGCAGGACGTTCCGGCAATC
CGCGACAAAATAAGGAAGCACCCCGCGGTCATCGACATCTACGAGTACGACATACCCTTCGCCAAGCGCTAC
CTCATAGACAAGGGCCTAATCCCGATGGAAGGTGAGGAAGAGCTTAAACTCATGTCCTTCGACATCGAGACG
CTCTACCACGAGGGAGAAGAGTTTGGAACCGGGCCGATTCTGATGATAAGCTACGCCGATGAAAGCGAGGCG
CGCGTGATAACCTGGAAGAAGATCGACCTTCCTTACGTTGAGGTTGTCTCCACCGAGAAGGAGATGATTAAG
CGCTTCTTGAGGGTCGTTAAGGAGAAGGACCCGGACGTGCTGATAACATACAACGGCGACAACTTCGACTTC
GCCTACCTGAAAAAGCGCTGTGAGAAGCTTGGCGTGAGCTTTACCCTCGGGAGGGACGGGAGCGAGCCGAAG
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AGGCGCACCATAAACCTCCCGACCTACACCCTTGAGGCTGTATACGAGGCGGTTTTCGGCAAGCCCAAGGAG
AAGGTCTACGCCGAGGAGATAGCCACCGCCTGGGAGACCGGCGAGGGGCTTGAGAGGGTCGCGCGCTACTCG
ATGGAGGACGCGAGGGGTTACCTACGAGCTTGGCAGGGAGTTCTTCCCGATGGAGGCCCAGCTTTCCAGGCTC
ATCGGCCAAGGCCTCTGGGACGTTTCCCGCTCCAGCACCGGCAACCTCGTCGAGTGGTTCCTCCTAAGGAAG
GCCTACGAGAGGAACGAACTCGCTCCCAACAAGCCCGACGAGAGGGAGCTGGCGAGGAGAAGGGGGGGCTAC
gcCGGTGGCTACGTCAAGGAGCCGGAGCGGGGACTGTGGGACAATATCGTGTATCTAGACTTTCGTAGTCTC
TACCCTTCAATCATAATCACCCACAACGTCTCGCCAGATACGCTCAACCGCGAGGGGTGTAGGAGCTACGAC
GTTGCCCCCGAGGTCGGTCACAAGTTCTGCAAGGACTTCCCCGGCTTCATTCCGAGCCTGCTCGGAAACCTG
CTGGAGGAAAGGCAGAAGATAAAGAGGAAGATGAAGGCAACTCTCGACCCGCTGGAGAAGAATCTCCTCGAT
TACAGGCAACGCGCCATCAAGATTCTCGCCAACAGCTACTACGGCTACTACGGCTATGCCAGGGCAAGATGG
TACTGCAGGGAGTGCGCCGAGAGCGTTACGGCATGGGGAAGGGAGTACATCGAAATGGTCATCAGAGAGCTT
GAGGAAAAGTTCGGTTTTAAAGTCCTCTATGCAGACACAGACGGTCTCCATGCCACCATTCCTGGAGCGGAC
GCTGAAACAGTCAAGAAAAAGGCAATGGAGTTCTTAAACTATATCAATCCCAAACTGCCCGGCCTTCTCGAA
CTCGAATACGAGGGCTTCTACGTCAGGGGCTTCTTCGTCACGAAGAAAAAGTACGCCGGTCATCGACGAGGAG
GGCAAGATAACCACGCGCGGGCTTGAGATAGTCAGGCGCGACTGGAGCGAGATAGCGAAGGAGACGCAGGCG
AGGGTTTTGGAGGCGATACTCAGGCACGGTGACGTTGAAGAGGCCGTCAGAATTGTCAGGGAAGTCACCGAA
AAGCTGAGCAAGTACGAGGTTCCGCCGGAGAAGCTGGTTATCCACGAGCAGATAACGCGCGAGCTCAAGGAC
TACAAGGCCACCGGCCCGCACGTAGCCATAGCGAAgcGTTTGGCCGCCAGAGGTGTTAAAATCCGGCCCGGA
ACTGTGATAAGCTACATCGTTCTGAAGGGCTCCGGAAGGATAGGCGACAGGGCGATTCCCTTCGACGAGTTC
GACCCGACGAAGCACAAGTACGATGCGGACTACTACATCGAGAACCAGGTTCTGCCGGCAGTTGAGAGAATC
CTCAGGGCCTTCGGCTACCGCAAGGAAGACCTGCGCTACCAGAAGACGAGGCAGGTCGGGCTTGGCGCGTGG
CTGAAGCCGAAGGGGAAGAAGAAGTGA

## FIG. 1

MILDVDYITENGKPVIRVFKKENGEFRIEYDREFEPYFYALLRDDSAIEEIKKITAERHGRVVKVKRAEKVK
KKFLGRSVEVWVLYFTHPQDVPAIRDKIRKHPAVIDIYEYDIPFAKRYLIDKGLIPMEGEEELKLMSFDIET
LYHEGEEFGTGPILMISYADESEARVITWKKIDLPYVEVVSTEKEMIKRFLRVVKEKDPDVLITYNGDNFDF
AYLKKRCEKLGVSFTLGRDGSEPKIQRMGDRFAVEVKGRVHFDLYPVIRRTINLPTYTLEAVYEAVFGKPKE
KVYAEEIATAWETGEGLERVARYSMEDARVTYELGREFFPMEAQLSRLIGQGLWDVSRSSTGNLVEWFLLRK
AYERNELAPNKPDERELARRRGGYAGGYVKEPERGLWDNIVYLDFRSLYPSIIITHNVSPDTLNREGCRSYD
VAPEVGHKFCKDFPGFIPSLLGNLLEERQKIKRKMKATLDPLEKNLLDYRQRAIKILANSYYGYYGYARARW
YCRECAESVTAWGREYIEMVIRELEEKFGFKVLYADTDGLHATIPGADAETVKKKAMEFLNYINPKLPGLLE
LEYEGFYVRGFFVTKKKYAVIDEEGKITTRGLEIVRRDWSEIAKETQARVLEAILRHGDVEEAVRIVREVTE
KLSKYEVPPEKLVIHEQITRELKDYKATGPHVAIAKRLAARGVKIRPGTVISYIVLKGSGRIGDRAIPFDEF
DPTKHKYDADYYIENQVLPAVERILRAFGYRKEDLRYQKTRQVGLGAWLKPKGKKK

# FIG. 2

MILDVDYITENGKPVIRVFKKENGEFRIEYDREFEPYFYALLRDDSAIEE
IKKITAERHGRVVKVKRAEKVKKKFLGRSVEVWVLYFTHPQDVPAIRDKI
RKHPAVIDIYEYDIPFAKRYLIDKGLIPMEGEEELKLMSFDIETLYHEGE
EFGTGPILMISYADESEARVITWKKIDLPYVEVVSTEKEMIKRFLRVVKE
KDPDVLITYNGDNFDFAYLKKRCEKLGVSFTLGRDGSEPKIQRMGDRFAV      Extein 1
EVKGRVHFDLYPVIRRTINLPTYTLEAVYEAVFGKPKEKVYAEEIATAWE
TGEGLERVARYSMEDARVTYELGREFFPMEAQLSRLIGQGLWDVSRSSTG
NLVEWFLLRKAYERNELAPNKPDERELARRRGGYAGGYVKEPERGLWDNI
VYLDFRSLYPSIIITHNVSPDTLNREGCRSYDVAPEVGHKFCKDFPGFIP
SLLGNLLEERQKIKRKMKATLDPLEKNLLDYRQRAIKILAN

                                         SLLPGEWVA
VIEGGKLRPVRIGELVDGLMEASGERVKRDGDTEVLEVEGLYASPSTGSP
RKPAQCR*KP**GTAMPGKFTE*LSTPEGGLSVTRGHSLFAYRDASLWR*
RGRRRFKPGDLLAVPSG*PSRRGGRGSTSLNCSSNCPRRKRPTCHRHSGK
GRKNFFRGMLRTLRWIFGEEKTGGRPGATWSTLRGLGYVKLRKIGYGVVD
REGLGKVPRFYERLVEVIRYNGNRGEFIADFNALRPVLRLMMPEKELEEW      Intein 1
LVGTRNGFRIRPFIEVDWKFAKLLGYYVSEGSAGKWKNRTGGWSYSVRLY
NEDGSVLDDMERLARSSLGA*ARGELRRDFKEDGLHNLRGALRFTGREQE
GSVAYLHVP*GGPLGLP*GVLHRRRRRSPEQDGSALHQERASG*RPRPAP
ELAGRLSDKRPPRQRGLQGLRERGTALYRVPEAEERLTYSHVIPREVLEE
TSAGPSRRT*VTGNSGSWWKAGSSTRKGPVG*AGSSTGI*SSTGSRKSGR
KATRGTSTT*ALRRTRTSGGLWVPLRAQX

                              SYYGYYGYARARWYCRECAES
VTAWGREYIEMVIRELEEKFGFKVLYADTDGLHATIPGADAETVKKKAME
FLNYINPKLPGLLELEYEGFYVRGFFVTKKKYAVIDEEGKITTRGLEIVR
RDWSEIAKETQARVLEAILRHGDVEEAVRIVREVTEKLSKYEVPPEKLVI      Extein 2
HEQITRELKDYKATGPHVAIAKRLAARGVKIRPGTVISYIVLKGSGRIGD
RAIPFDEFDPTKHKYDADYYIENQVLPAVERILRAFGYRKEDLRYQKTRQ
VGLGAWLKPKGKKK

# FIG. 3

AATTCCACTGCCGTGTTTAACCTTTCCACCGTTGAACTTGAGGGTGATTT
TCTGAGCCTCCTCAATCACTTAATCGAGACCGCGGATTACCTTGAACTGG
TACACGTTCAACGATTCGGTTCTTGTAATGGTCGATACTGGGCCGTGCTG
GATTTTCTAAACGTCTCAAGAACGGCTTTCATCAACGGAAACTGCCACGT   5' untranslated sequence
CTCCGCCGTCGTGAGGGTTAAACCTGAAGTTCAAGACTTTGCAACGGAAT
GGCGAGAGAACGGCGACTACCCCAGTGGAAGAGCTTTTGAAAGCCAAAGC
CGAGCTTCAGCGAATGTGCGGTGCCCTTGTTCAAGAGTTGTGAGCCCTTG
ATTGTTGTTTTCTCCTCTTTTCTGATAACATCGATGGCGAAGTTTATTAG
TTCTCAGTTCGATAATCAGGCAGGTGTTGGTC

                                   ATGATCCTTGACGTTGAT
TACATCACCGAGAATGGAAAGCCCGTCATCAGGGTCTTCAAGAAGGAGAA
CGGCGAGTTCAGGATTGAATACGACCGCGAGTTCGAGCCCTACTTCTACG
CGCTCCTCAGGGACGACTCTGCCATCGAAGAAATCAAAAAGATAACCGCG
GAGAGGCACGGCAGGGTCGTTAAGGTTAAGCGCGCGGAGAAGGTGAAGAA
AAAGTTCCTCGGCAGGTCTGTGGAGGTCTGGGTCCTCTACTTCACGCACC
CGCAGGACGTTCCGGCAATCCGCGACAAAATAAGGAAGCACCCCGCGGTC
ATCGACATCTACGAGTACGACATACCCTTCGCCAAGCGCTACCTCATAGA
CAAGGGCCTAATCCCGATGGAAGGTGAGGAAGAGCTTAAACTCATGTCCT
TCGACATCGAGACGCTCTACCACGAGGGAGAAGAGTTTGGAACCGGGCCG
ATTCTGATGATAAGCTACGCCGATGAAAGCGAGGCGCGCGTGATAACCTG
GAAGAAGATCGACCTTCCTTACGTTGAGGTTGTCTCCACCGAGAAGGAGA
TGATTAAGCGCTTCTTGAGGGTCGTTAAGGAGAAGGACCCGGACGTGCTG
ATAACATACAACGGCGACAACTTCGACTTCGCCTACCTGAAAAAGCGCTG
TGAGAAGCTTGGCGTGAGCTTTACCCTCGGGAGGGACGGGAGCGAGCCGA   Extein 1
AGATACAGCGCATGGGGGACAGGTTTGCGGTCGAGGTGAAGGGCAGGGTA
CACTTCGACCTTTATCCAGTCATAAGGCGCACCATAAACCTCCCGACCTA
CACCCTTGAGGCTGTATACGAGGCGGTTTTCGGCAAGCCCAAGGAGAAGG
TCTACGCCGAGGAGATAGCCACCGCCTGGGAGACCGGCGAGGGGCTTGAG
AGGGTCGCGCGCTACTCGATGGAGGACGCGAGGGGTTACCTACGAGCTTGG
CAGGGAGTTCTTCCCCGATGGAGGCCCAGCTTTCCAGGCTCATCGGCCAAG
GCCTCTGGGACGTTTCCCGCTCCAGCACCGGCAACCTCGTCGAGTGGTTC
CTCCTAAGGAAGGCCTACGAGAGGAACGAACTCGCTCCCAACAAGCCCGA
CGAGAGGGAGCTGGCGAGGAGAAGGGGGGGCTACGCCGGTGGCTACGTCA
AGGAGCCGGAGCGGGGACTGTGGGACAATATCGTGTATCTAGACTTTCGT
AGTCTCTACCCTTCAATCATAATCACCCACAACGTCTCGCCAGATACGCT
CAACCGCGAGGGGTGTAGGAGCTACGACGTTGCCCCCGAGGTCGGTCACA
AGTTCTGCAAGGACTTCCCCGGCTTCATTCCGAGCCTGCTCGGAAACCTG
CTGGAGGAAAGGCAGAAGATAAAGAGGAAGATGAAGGCAACTCTCGACCC
GCTGGAGAAGAATCTCCTCGATTACAGGCAACGCGCCATCAAGATTCTCG
CCAAC

<div align="center">FIG. 4</div>

AGCCTTCTTCCCGGGGAGTGGGTTGCGGTCATTGAAGGGGGGAAA
CTCAGGCCCGTCCGCATCGGCGAGCTGGTTGATGGACTGATGGAAGCCAG
CGGGGAGAGGGTGAAAAGAGACGGCGACACCGAGGTCCTTGAAGTCGAGG
GGCTTTACGCCTCTCCTTCGACAGGGAGTCCAAGAAAGCCCGCACAATGC
CGGTGAAAGCCGTGATAAGGCACCGCTATGCCGGGGAAGTTTACAGAATA
GCTCTCAACTCCGGAAGGAGGATTAAGCGTGACGCGCGGCCACAGCCTCT
TCGCGTACCGGGACGCGAGCTTGTGGAGGTGACGGGGGAGGAGGAGGTTC
AAGCCCGGCGACCTCCTGGCGGTGCCAAGCGGATAACCCTCCCGGAGAGG
AGGGAGAGGCTCAACATCGTTGAACTGCTCCTCGAACTGCCCGAGGAGGA

AACGGCCGACATGTCATCGACATTCCGGCAAGGGTAGAAAGAACTTCTTC
AGGGGAATGCTCAGAACCCTCCGCTGGATTTTCGGGGAGGAGAAGACCGG Intein 1
AGGGCGGCCAGGCGCTACCTGGAGCACCTTGCGTGGGCTCGGCTACGTGA
AGCTGAGGAAAATCGGCTACGGGGTGGTTGATAGGGAGGGACTGGGAAAG
GTACCGCGCTTCTACGAGAGGCTCGTGGAGGTAATCCGCTACAACGGCAA
CAGGGGGGAGTTCATCGCCGATTTCAACGCGCTCCGCCCCGTCCTCCGCC
TGATGATGCCCGAGAAGGAGCTTGAAGAGTGGCTCGTTGGGACGAGGAAC
GGGTTCAGGATAAGGCCGTTCATAGAGGTTGATTGGAAGTTCGCAAAGCT
CCTCGGCTACTACGTGAGCGAGGGGAGCGCCGGGAAGTGGAAAAACCGGA
CCGGGGGCTGGAGCTACTCGGTGAGGCTTTACAACGAGGACGGGAGCGTT
CTCGACGACATGGAGAGACTCGCGAGGAGTTCTTTGGGGGCGTGAGCGCG
GGGGGAACTACGTCGAGATTTCAAAGAAGATGGCCTACATAATCTTCGAG
GGGCTCTGCGGTTCACCGGCCGAGAACAAGAGGGTTCCGTGGCTTATCTT
CACGTCCCCTGAGGAGGTCCGCTGGGCCTTCCTTGAGGGGTACTTCATCG
GCGACGGCGACGTTCACCCGAGCAAGATGGTTCGGCTCTCCACCAAGAGC
GAGCTTCTGGCTAACGGCCTCGTCCTGCTCCTGAACTCGCTGGGCGTCTC
AGCGATAAACGTCCGCCACGACAGCGGGGTTTACAGGGTCTACGTGAACG
AGGAACTGCCCTTTACAGAGTACCGGAAGCGGAAGAACGCCTCACTTACT
CCCACGTCATACCGAGGGAAGTGCTGGAGGAGACTTCGGCCGGGCCTTCC
AGAAGAACATGAGTCACGGGAAATTCAGGGAGCTGGTGGAAAGCGGGGAG
CTCGACGCGGAAAGGGCCGGTAGGATAGGCTGGCTCCTCGACGGGGATAT
AGTCCTCGACAGGGTCTCGGAAGTCAGGAAGGAAAGCTACGAGGGGTACG
TCTACGACCTGAGCGTTGAGGAGGACGAGAACTTCTGGCGGGCTTTGGGT
TCCTCTACGCGCACAACNN

# FIG. 4 (cont.)

AGCTACTACGGCTACTACGGCTATGCCAGGG
CAAGATGGTACTGCAGGGAGTGCGCCGAGAGCGTTACGGCATGGGGAAGG
GAGTACATCGAAATGGTCATCAGAGAGCTTGAGGAAAAGTTCGGTTTTAA
AGTCCTCTATGCAGACACAGACGGTCTCCATGCCACCATTCCTGGAGCGG
ACGCTGAAACAGTCAAGAAAAAGGCAATGGAGTTCTTAAACTATATCAAT
CCCAAACTGCCCGGCCTTCTCGAACTCGAATACGAGGGCTTCTACGTCAG
GGGCTTCTTCGTCACGAAGAAAAAGTACGCGGTCATCGACGAGGAGGGCA
AGATAACCACGCGCGGGCTTGAGATAGTCAGGCGCGACTGGAGCGAGATA
GCGAAGGAGACGCAGGCGAGGGTTTTGGAGGCGATACTCAGGCACGGTGA  Extein 2
CGTTGAAGAGGCCGTCAGAATTGTCAGGGAAGTCACCGAAAAGCTGAGCA
AGTACGAGGTTCCGCCGGAGAAGCTGGTTATCCACGAGCAGATAACGCGC
GAGCTCAAGGACTACAAGGCCACCGGCCCGCACGTAGCCATAGCGAAGCG
TTTGGCCGCCAGAGGTGTTAAAATCCGGCCCGGAACTGTGATAAGCTACA
TCGTTCTGAAGGGCTCCGGAAGGATAGGCGACAGGGCGATTCCCTTCGAC


GAGTTCGACCCGACGAAGCACAAGTACGATGCGGACTACTACATCGAGAA
CCAGGTTCTGCCGGCAGTTGAGAGAATCCTCAGGGCCTTCGGCTACCGCA
AGGAAGACCTGCGCTACCAGAAGACGAGGCAGGTCGGGCTTGGCGCGTGG
CTGAAGCCGAAGGGGAAGAAGAAGTGA


                              GGAATTATCTGGTTTCTTTTCCC
AGCATTAAATGCTTCCGACATTGCCTTATTTATGAAACTCCTGTTGTGCC
TGAGTTTGTGCCAGAAAACAGCCTGTTCTGACGGCGCTTTTTCTTGCCAG
GTCTCTTGAGTTTCGCAAGGGTCTTCTCGACCAGCTCAATGGTCTTGTCG
TCATTGTTTNNNNNNNNNNNNNNNNNNNNNNNNNCCCGGGGACTTCATACTGGC
GGTAATAGACAGGGATTCCTTCCTCAAGGACTTCCCGGGAGGCATTGGAG
TTTTTTGGTGGGGCTTTCACAGGATTTGCTCATCTTGTGGATTTCTCGTT
CGATTGAATCTGTCCACTTGAGGGTGTAGGTCGAGACGGTGGAGCGCGTA
TTCCGGGAGCGGGTCTTGAGGCTCCATTTTTCAGTCCTCCTCCGGCGAAG  3' Untranslated sequence
AAGTGGAACTCAAGCCGGGTGTTAGCTTATGTTATGTTCCCAACTCCTCC
AGCACCTCCAGGATCCCCTCAATCCCGGAACCTCGAAGCCCCTCTCGTGG
ATCTTTCTAACTTCCTCTGCCTCCGGGTTTATCCAGACCGCCCACATGCC
GGCTCTCAGCGCACCCTCGAAATCCTCCGCGTAGGTGTCGCCGATGTGGA
TTGCCTCGTCCGGCTCGACCCCGAAGCATCGAGCGGTTTTCTGAACATCT
CGGGCATCGGCTTATACGCCAGAACCTCGTCGGCGAAGAAGGTTCCCTCA
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GCCCTATAGTGAGTCGATTACAATTCACTGGCCGTCGTTTTACAACGTCG
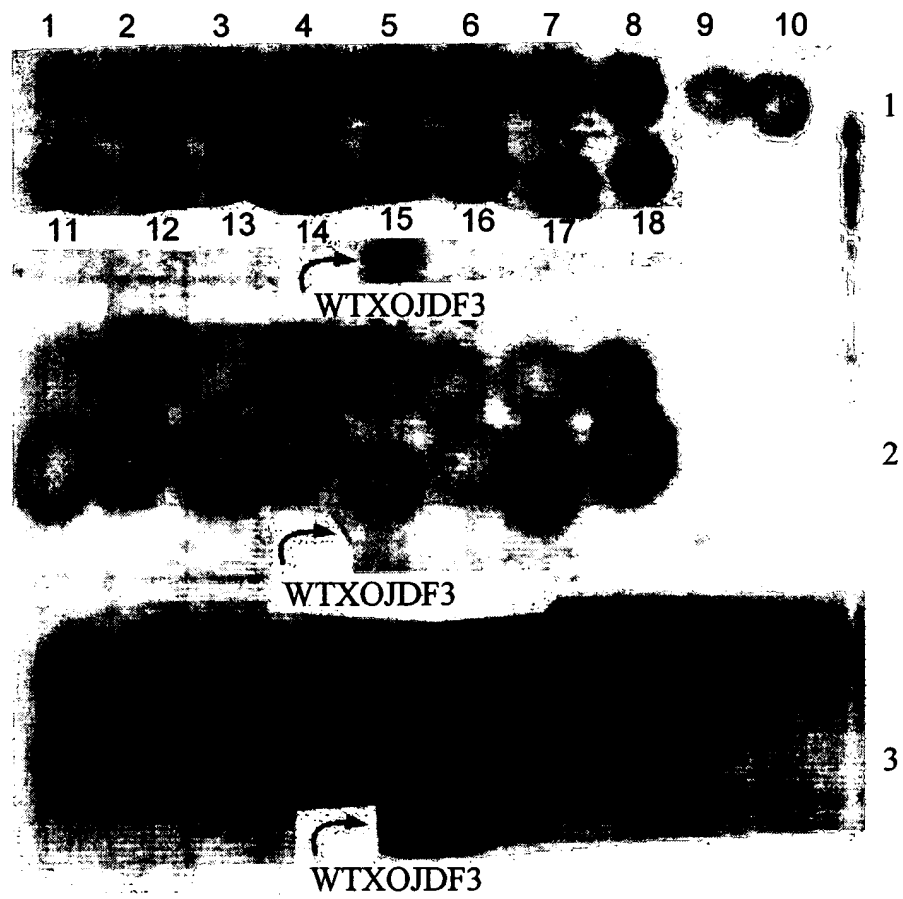TGACTGGGAAAACCCTGGCGTTACCCAACTTAAGTCGCTTTGCAGCACAT
CCCCC


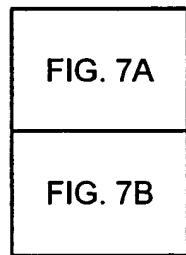FIG. 4 (cont.)

FIG. 5

Sequencing with Purified Mutants



A

B

C

D

E

FIG. 6

FIG. 7A

FIG. 7B

FIG. 7

Sequencing with Dye-labeled Dideoxynucleotides



FIG. 7A
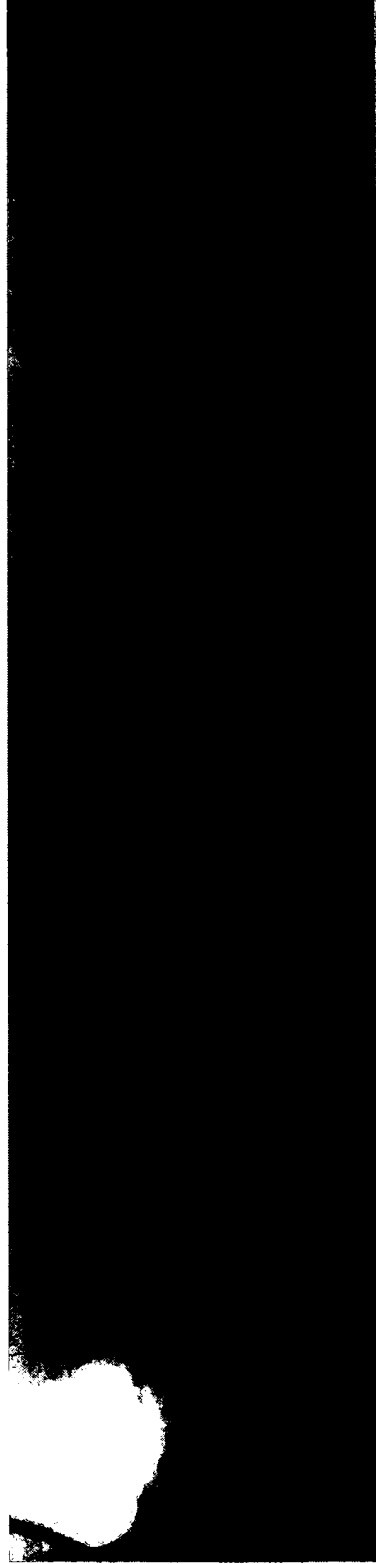
FIG. 7B

Sequencing with the P410L, A485T Double Mutant and α-$^{33}$ P Dideoxynucleotides
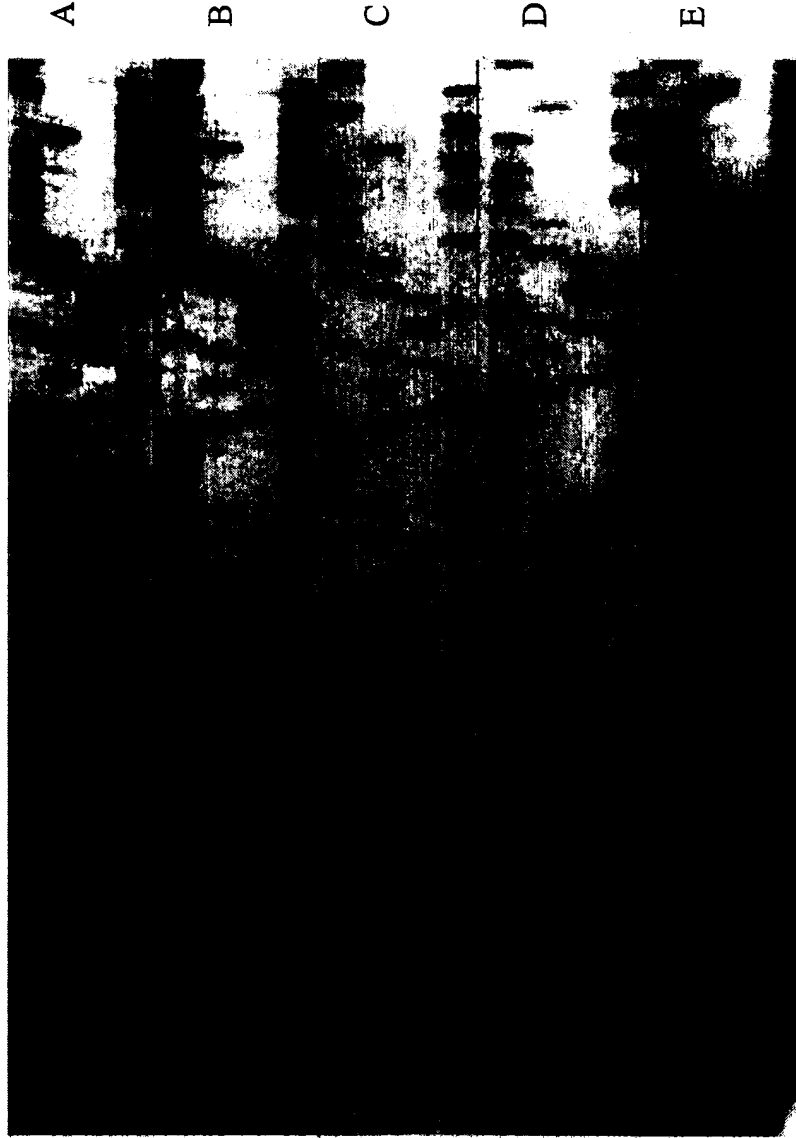
FIG. 8
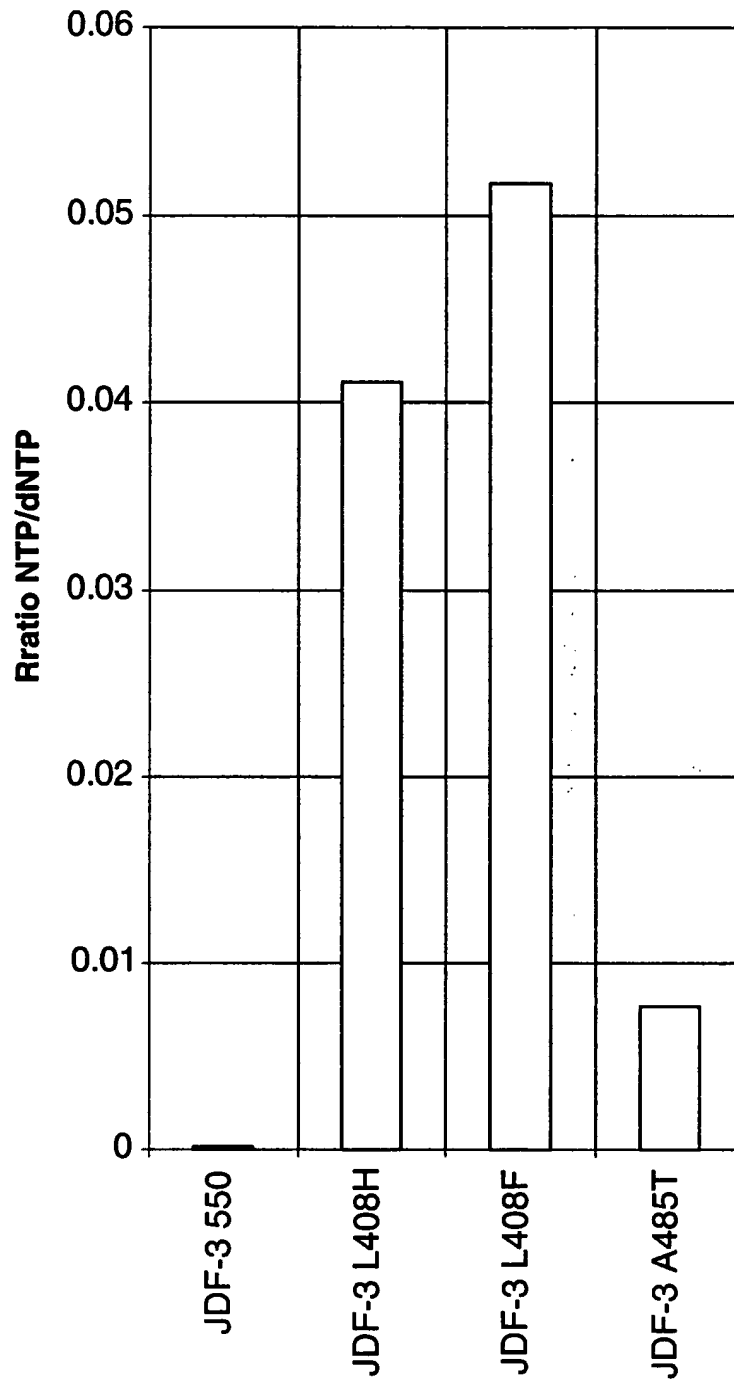
FIG. 9
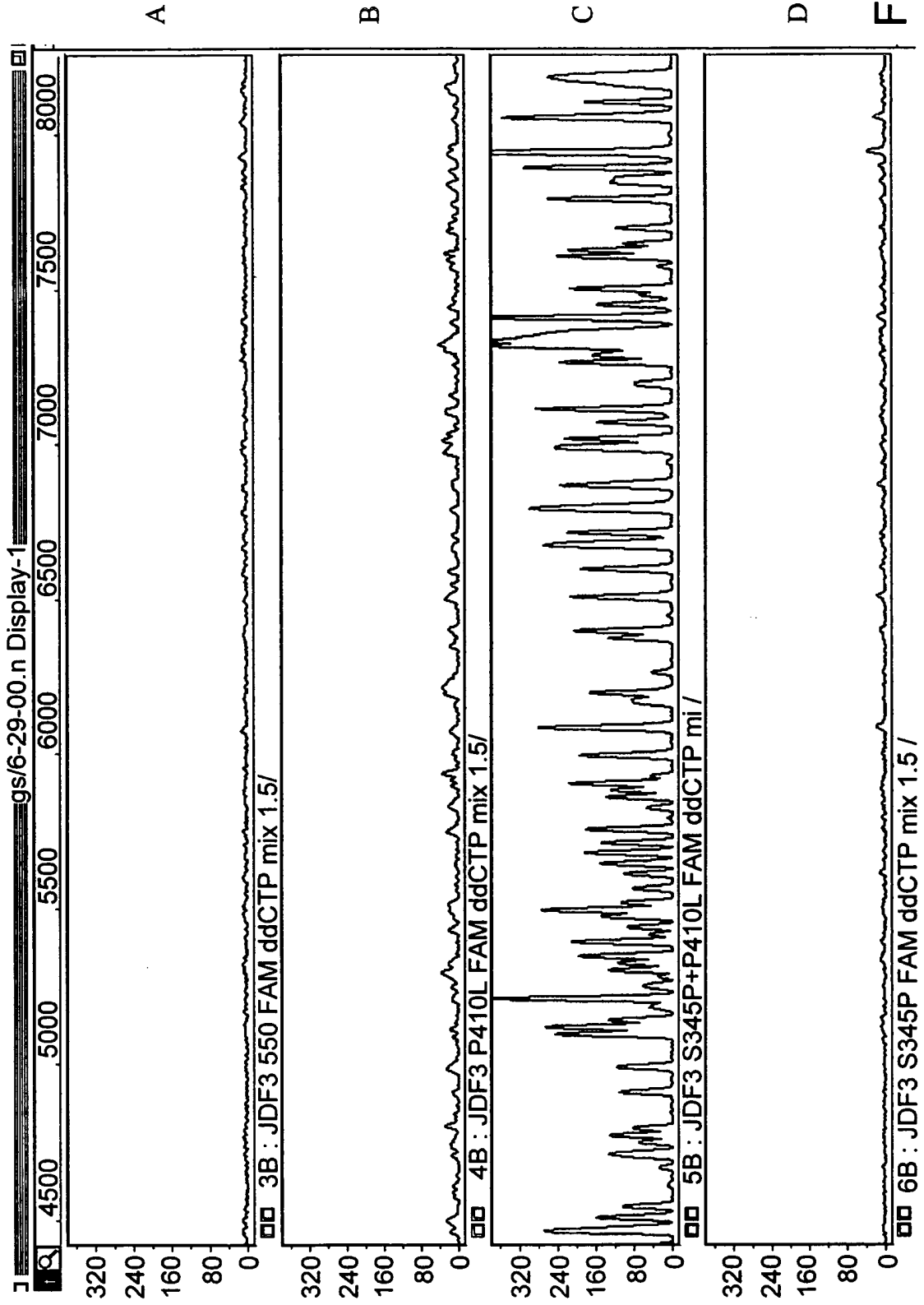
A

B    3B : JDF3 550 FAM ddCTP mix 1.5/

C    4B : JDF3 P410L FAM ddCTP mix 1.5/

D    5B : JDF3 S345P+P410L FAM ddCTP mi /

   6B : JDF3 S345P FAM ddCTP mix 1.5/

gs/6-29-00.n Display-1

FIG. 10

A

2B : TS FAM ddCTP mix 1.5 /

B

5B : JDF3 S345P + P410L FAM ddCTP mi /

FIG. 11
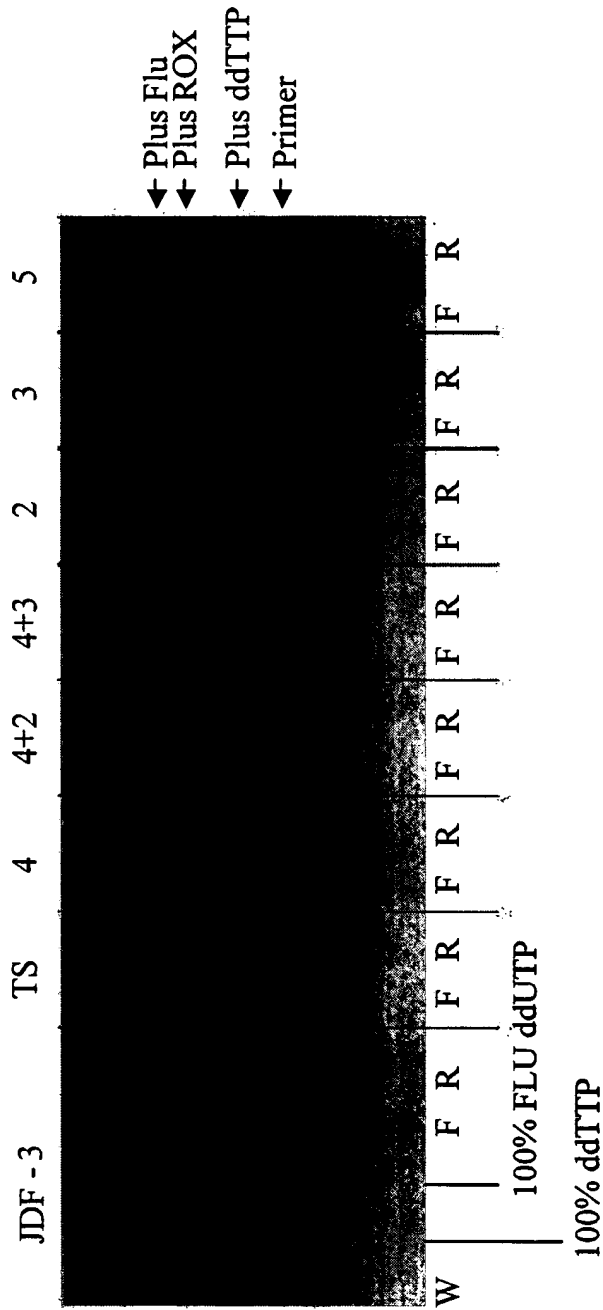
FIG. 12
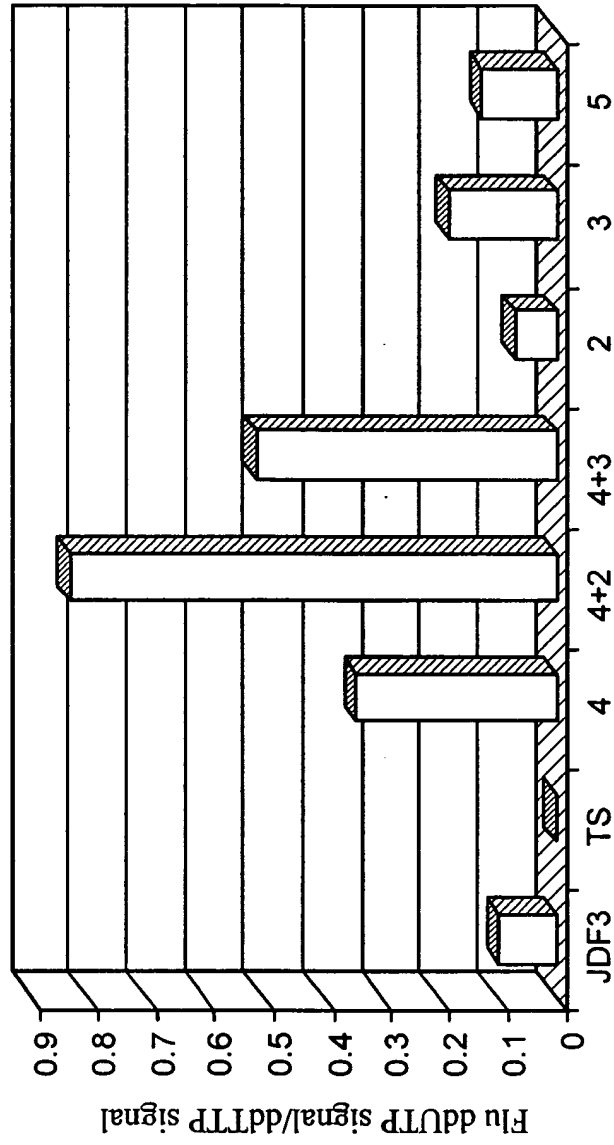
**FIG. 13**

Shading removed. Mutations indicated by underlining

```
4     1  -----------------------------------------------LVXNAXSTGNLVEWFLLRK
10    1  -----------------------------------------------VWDVSRSSTGNLVERFLLRK
13    1  -----------------------------------------------VWDVSRSSTGNLVEWFLLRK
16    1  -----------------------------------------------VWDVSRSSTGNLVEWFLLRK
18    1  -----------------------------------------------VWDVSRSSTGNLVEWFLLRK
19    1  -----------------------------------------------VWDVXRSSTGNLVEWFLLRK
28    1  -----------------------------------------------VWDVPRSSTGNLVEWFLLRK
34    1  -----------------------------------------------VWDVSRSSTGNLVEWFLLRK
41    1  -----------------------------------------------VWDVSRSSTGNLVEWFLLRK
33    1  -----------------------------------------------VWDVSRSSTGNLVEWFLLRK
48    1  --------------------------------------------YWSXPXLRTGNLVEWFLLRK
55    1  ---------------------------------------------VLGTXPRSSTGNLVEWFLLRK
64    1  -------------------------------------------XXXFWDVSRSSTGNLVEWFLLRK
Jdf3 301 TGEGLERVARYSMEDARVTYELGREFFPMEAQLSRLIGQGLWDVSRSSTGNLVEWFLLRK
             310       320       330       340       350       360

4    20  AYERNELAPNKPDERELARRRGGYAGGYVKEPERGLWDNIVYLDFRSLYPSIIITHNVSP
10   21  AYERNELAPNKPDERELARRRGGYAGGYVKEPERGLWDNIVYLDFRSLYPSIIITHSVSP
13   21  AYERNELAPNKPDERELARRRGGYAGGYVKEPERGLWDNIVYLDFRSLYPSIIITHNVSP
16   21  AYERNELAPNKPDERELARRRGGYAGGYVKEPERGLWDNIVYLDFRSLYPSIIITHNVSP
18   21  AYERNELAPNKPDERELARRRGGYAGGYVKEPERGLWDNIVYLDFRSLYPSIIITHNVSP
19   21  AYERNELAPNKPDERELARRRGGYAGGYVKEPERGQWDNIAYLDFRSLYPSIIITHNVSP
28   21  AYERNELAPNKPDERELARRRGGYAGGYVKEPERGLWDNIVYLDFRSLYPSIIITHNVSP
34   21  AYERNELAPNKPDERELARRRGGYAGGYVKEPERGLWDNIVYLDFRSLYPSIIITHNVSP
41   21  AYERNELAPNKPDERELARRRGGYAGGYVKEPERGPWDNIVYLDFRSLYPSIIITHNVSP
33   21  AYERNKLAPNKPDERELARRRGGYAGGYVKEPERGLWDNIVYLDFRSLYPSIIITHNVSP
48   21  AYERNELAPNKPDERELARRRGGYAGGYVKEPERGLWDNIVYLDFRSLYPSIIITHNVSP
55   22  AYERNELAPNKPDERELARRRGGYAGGYVKEPERGLWDNIVYLDFRSHYPSIIITHNVSP
64   24  AYERNELAPNKPDERELARRRGGYAGGYVKEPERGLWDNIVYLDFRSLYPSIIITHNVSP
Jdf3 361 AYERNELAPNKPDERELARRRGGYAGGYVKEPERGLWDNIVYLDFRSLYPSIIITHNVSP
             370       380       390       400       410       420
```
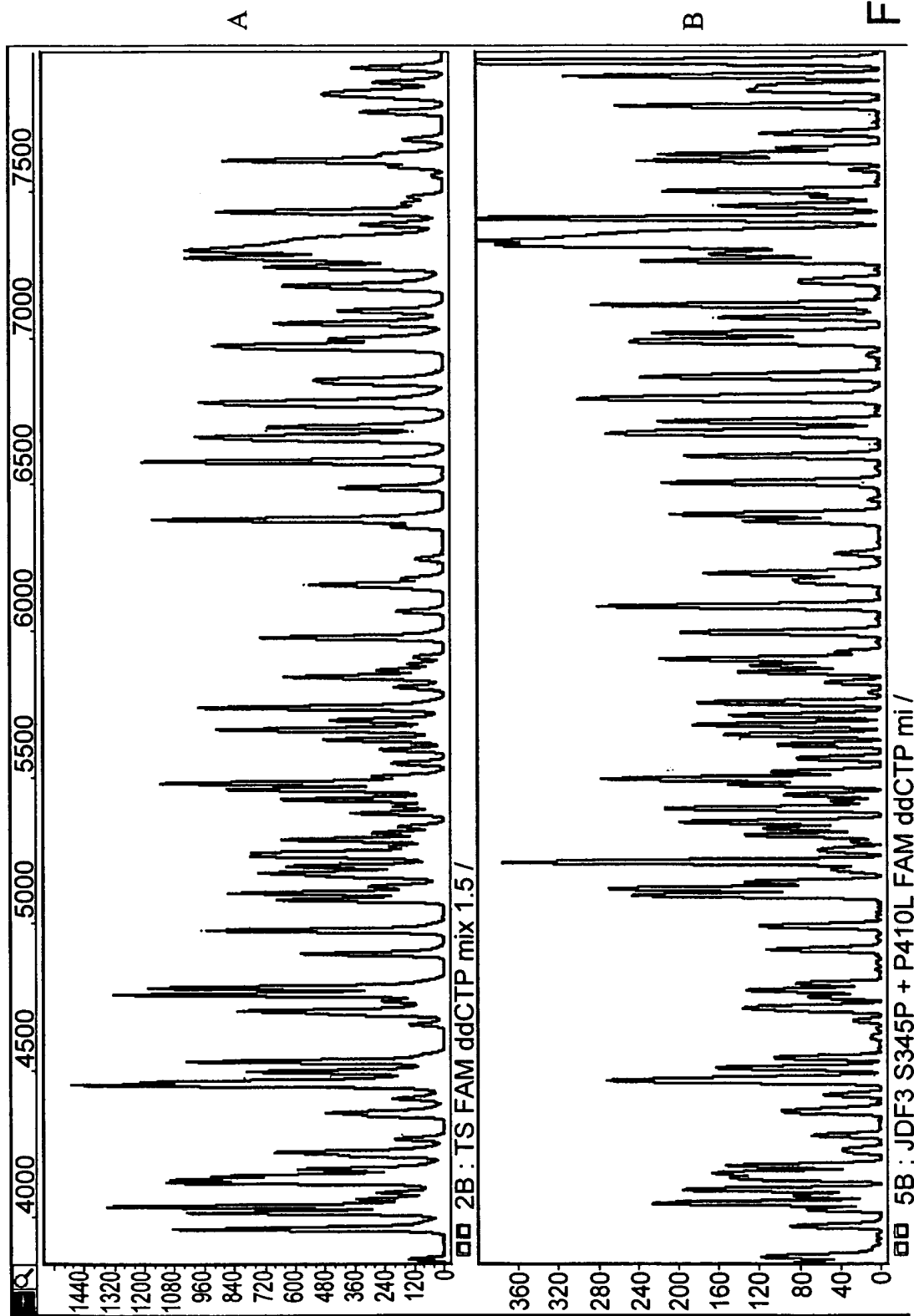
FIG. 14

Shading Removed -
Mutations indicated by
Underlining

```
4     80  DTLNREGCRSYDVAPEVGHKFCKDFPGFIPSLLGNLLEERQKIKRKMKATLDPLEKNLLD
10    81  DTLDREGCRSYDVAPEVGHKFCKDFPGFIPSLLGNLLEERQKIKRKMKATLDPLEKNLLD
13    81  DTLNREGCRSYDVAPEVGHKFCKDFPGFIPSLLGNLLEERQKIKRKMKATLDPLEKNLLD
16    81  DTLNREGCRSYDVAPEVGHKFCKDFPGFIPSLLGNLLEERQKIKMKMKATLDPLEKNLLD
18    81  DTLNREGCRSYDVAPEVGHKFCKDFPGFIPSLLGNLLEERQKIKRKMKATLDPLEKNLLD
19    81  DTLKREGCRSYDVAPEVGHKFCKDFPGFIPSLLGNLLEERQKIKRKMKATLDPLEKNLLD
28    81  DTLNREGCRSYDVAPEVGHKFCKDFPGFIPSLLGNLLEERQKIKRKMKATLDPLEKNLLD
34    81  DTLNREGCRSYXVAPEVGHKFCKDFPGFIPSLLGNLLEERQKIKRKMKATLDPLEKNLLD
41    81  DTLNREGCRSYXVAPEVGHKFCKDFPGFIPSLLGNLLEVRQKIKRKMKATLDPLEKNLLD
33    81  DTLNREGCRSYDVAPEVGHKFCKDFPGFIPSLLGNLLEERQKIKRKMKATLDPLEKNLLD
48    81  DTLNREGCRSYDVAPEVGHKFCKDFPGFIPSLLGNPLEERQKIKRKMKATLDPLEKNLLD
55    82  DTLNREGCRSYDVAPEDGHKFCKDFPGFIPSLLGNLLEERQKIKRKMKATLDPLEKNHLD
64    84  DTLNREGCRSYDVAPEVGHKFCKDFPGFIPSLLGNLLEERQKIKRKMKATLDPLEKNLLD
Jdf3 421  DTLNREGCRSYDVAPEVGHKFCKDFPGFIPSLLGNLLEERQKIKRKMKATLDPLEKNLLD
                430       440       450       460       470       480
```

FIG. 14 (cont.)

*Shading removed — mutations indicated by underlining*

| | | |
|---|---|---|
| 4 | 140 | YRQRAIKILANSYYGY<u>C</u>GYARARWYCRECAESVTAWGREYIEMVIRELEEKFGFKVLYAD |
| 10 | 141 | YRQRAIKILANSYYGYYGYARARWYCRECAESVTAWGREYIEMVIRELEEKFGFKVLYAD |
| 13 | 141 | YRQRAIKILANSYYGYYGYARARWYCRECAESVTAWGREYIEMVIRELEEKFGFKVLYAD |
| 16 | 141 | YRQRAIKILANSYYGYYGYARARWYCRECAESVTAWGREYIEMVIRELEEKFGFKVLYAD |
| 18 | 141 | YRQRAIKILAN<u>N</u>YYGYYGYARARWYCRECAESVTAWGREYIEMVIRELEEKFGFKVLYAD |
| 19 | 141 | YRQRAIKILANSYYGYYGYARARWYCRECAESVTAWGREYIEMVIRELEEKFGFKVLYAD |
| 28 | 141 | YRQRAIKILANSYYGYYGYARARWYCRECAESVTAWGREYIEMVIRELEEKFGFKVLYAD |
| 34 | 141 | YRQRAIKILANSYYGYYGYARARWYCRECAESVTAWGREYIEMVIRELEEKFGFKVLYAD |
| 41 | 141 | YRQRAIKILANSYYGYYGYARARWYCRECAESVTAWGREYIEMVIRELEEKFGFKVLYAD |
| 33 | 141 | YRQRAIKILANSYYGYYGYARARWYCRECAESVTAWGREYIEMVIRELEEKFGFKVLYAD |
| 48 | 141 | YRQRAIKILANSYYGYYGYARARWYCRECAESVTAWGREYIEMVIRELEEKFGFKVLYAD |
| 55 | 142 | YRQRAIKILANSYYGYYGYARARWYCRECAESVTAWGREYIEMVIRELEEKFGFKVLYAD |
| 64 | 144 | YRQRAIKILANSYYG<u>N</u>YGYARARWYCRECAESVTAWGREYIEMVIRELEEKFGFKVLYAD |
| Jdf3 | 481 | YRQRAIKILANSYYGYYGYARARWYCRECAESVTAWGREYIEMVIRELEEKFGFKVLYAD |
| | | 490       500 |

| | | |
|---|---|---|
| 4 | 200 | TDGLHATIPGADAETVKKKAMEFLNYINPKLPGLLELEYEGFYVRGFFVTKKKYAVIDEE |
| 10 | 201 | TDGLHATIPGADAETVKKKAMEFLNYINPKLPGLLELEYEGFYVRGFFVTKKKYAVIDEE |
| 13 | 201 | TDGLHATIPGADAETVKKKAMEFLNYINPKLPGLLELEYEGFYVRGFFVTKKKYAVIDEE |
| 16 | 201 | TDGLHATIPGADAETVKKKAMEFLNYINPKLPGLLEL<u>K</u>YEGFYVRGFFVTKKKYAVIDEE |
| 18 | 201 | TDGLHATIPGADAETVKKKAMEFLNYINPKLPGLLELEYEGFYVRGFFVTKKKYAVIDEE |
| 19 | 201 | TDGLHATIPGADAETVKKKAMEFLNYIN<u>L</u>KLPGLLELEYEGFYVRGFFVTKKK<u>X</u>AVIDEE |
| 28 | 201 | TDGLHATIPGADAETVKKKAMEFLNYINPKLPGLLELEYEGFYVRGFFVTKKKYAVIDEE |
| 34 | 201 | TDGLHATIPGADAETVKKKAMEFLNYINPKLPGLLELEYEGFYVRGFFVTKKKYAVIDEE |
| 41 | 201 | TDGLHATIPGADAETVKKKAMEFLNYINPKLPGLLELEYEGFYVRGFFVTKKKYAVIDEE |
| 33 | 201 | TDGLHATIPGADAETVKKKAMEFLNYINPKLPGLLE<u>P</u>EYEGFYVRGFFVTKKKYAVIDEE |
| 48 | 201 | TDGLHATIPGADAETVKKKAMEFLNYINPKLPGLLELEYEGFYVRGFFVTKKKYAVIDEE |
| 55 | 202 | TDGLHATIPGADAETVKKKAMEFLNYINPKLPGLLELEYEGFYVRGFFVTKKKYAVIDEE |
| 64 | 204 | TDGLHATIPGADAETVKKKAMEFLNYINPKLPGLLELEYEGFYVRGFFVTKKKYAVIDEE |
| Jdf3 | 541 | TDGLHATIPGADAETVKKKAMEFLNYINPKLPGLLELEYEGFYVRGFFVTKKKYAVIDEE |
| | | 550   560   570   580   590   600 |

## FIG. 15

Shading removed –
Mutations indicated
by underlining

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4     260 GKITTRGLEIVRRDWSEIAKETQARVLEAVLRHGDVEEAVRIVREVTEKLSKYEVPPEKL
10    261 GKITTRGLEIVRRDWSEIAKETQARVLEAILRHGDVEEAVRIVREVTEKLSKYEVPPEEL
13    261 GKITTRGLEIVRRDWSEIAKETQARVLEAILRHGDVEEAVRIVRKVTEKLSKYEVPPEKL
16    261 GKITTRGLEIVRRDWSEIAKETQARVLEAILRHGDVEEAVRIVREVTEKLSKYEVPPEKL
18    261 GKITTRGLEIVRRDWSEIAKETQARVLEAILRHDDVEEAVRIVREVTEKLSKYEVPPEKL
19    261 GKITTRGLEIVRRDWSKIAKETQARVLEAILRHGDVEEAIRIVREVTEKLSKYEVPPEKL
28    261 GKIATRGLEIVRRDWSEIAKETQARVLEAILRHGDVEEAVRIVREVTEKLSKYEVPPEKL
34    261 GKITTRGLEIVRRDWSEIAKETQARVLEAILRHGDVEEAVRIVREVTEKLNKYEVPPEKL
41    261 GKITTRGLEIVRRDWSEIAKETQARVLEAILRHGDVEEAVRIVREVTEKLSKYEVPPEKL
33    261 GKITTRGLEIVRRDWSEIAKETQARVLEAILRHGDVEEAVRIVREVTEKLSKYEVPPEKL
48    261 GKITTRGLEIVRRDWSEIAKETQARVLEAILRHGDVEEAVRIVREVTEKLSKYEVPPVKL
55    262 GKITTRGLEIVRRDWSEIAKETQARVLEAILRHGDVEEAVRIVREVTEKLSKYEVPPGEA
64    264 GKITTRGLEIVRRDWSEIAKETQARVLEAILRHGDVEEAVRIVREVTEKLSKYEVPPEKL
Jdf3  601 GKITTRGLEIVRRDWSEIAKETQARVLEAILRHGDVEEAVRIVREVTEKLSKYEVPPEKL
              610       620       630       640       650       660
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FIG. 15 (cont.)